REMARKS

With this Amendment claim 1 has been amended; claims 4 and 13 have been cancelled, and claim 14 has been added. Claims 1-3, 6-12, and 14 are pending. Claims 2-3, 10, and 12 are withdrawn. Reconsideration and allowance of the application are respectfully requested.

Support for the Amendment can be found throughout the specification and original claims, e.g., at pages 5-7, paragraphs [0023] – [0025]; page 13, paragraphs [0045] – [0046]; Figure 1; and original claim 4. Applicants note that SEQ ID NOs: 7-12 each have one substitution with respect to SEQ ID NO: 1. SEQ ID NO: 13 has two substitutions with respect to SEQ ID NO: 1.

Response To Rejection Under 35 U.S.C. § 112, 2nd Paragraph

The Office Action rejects claims 1, 4, 6-9, 11, and 13 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In particular, the Office Action rejects claim 1 for recitation of "DNA of the nucleotide sequence represented by SEQ ID NO: 1 having two to five base modifications chosen from base substitutions, deletions, additions, and insertions". The Office Action further rejects claim 13 as allegedly indefinite with respect to the relative positions of the specific substitutions recited in the claim.

In response, and without acquiescing to the propriety of the rejection, Applicants submit that the present Amendment is responsive to the instant rejections. In particular, Applicants submit that claim 1 has been amended such that it is even clearer and more definite, and that one of ordinary skill in the art would immediately know the metes and bounds of the claimed subject matter. Applicants further submit that the rejection is moot with respect to claim 13, as claim 13 has been cancelled.

Accordingly, Applicants respectfully request reconsideration of the instant rejections under 35 U.S.C. § 112, second paragraph, and withdrawal the same.

Response To Rejection Under 35 U.S.C. § 112, 1st Paragraph

The Office Action maintains the rejection of claims 1, 4, 6-9, 11, and 13 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Action alleges that Applicants (1) do not describe any DNAs 'derived from' SEQ ID NO: 1 that function as an IRES, and (2) do not describe SEQ ID NO:1 as having IRES activity in any plant other than *Arabidopsis*.

The Office Action further asserts that Applicants' previous arguments have been found unpersuasive. In particular, the Office Action asserts that Applicants' previous argument that the specification describes 16 variants of SEQ ID NO: 1 with IRES activity in plants, is not persuasive, allegedly because none of the 16 variants "are *shown* to have IRES activity" (Office Action at page 7, last paragraph; emphasis added). The Office Action further concedes that Applicants have disclosed two different constructs comprising repeats of SEQ ID NO: 1 having IRES activity in *Arabidopsis* (Office Action at page 8, first paragraph). However, the Office Action then asserts that none of the claims are limited in scope to such constructs. *Id.* In addition, the Office Action states that Applicants' arguments regarding the description of plants belonging to various families to be transformed with the disclosed IRES sequences were not persuasive because the claimed nucleic acids were allegedly "not shown to have IRES activity" in any plants other than *Arabidopsis* and because there is allegedly a high degree of unpredictability regarding IRES function as evidenced by Applicants' disclosure with respect to

the effect on expression of the ECMV IRES (Office Action at page 8, second paragraph; emphasis added).

In response, Applicants submit that the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants further submit that the instant rejection appears *not* to be based upon this standard of possession, but rather on the improper assertion that Applicants' claimed subject matter must be limited to the working examples disclosed in the specification.

In particular, Applicants submit that the specification fully describes the claimed subject matter. For example, the specification provides working examples of two different constructs, including an example comprising ten repeats of SEQ ID NO: 1 without spacer sequences in between the repeats (specification at pages 21-22, paragraphs [0074] – [0075] and Figure 4). In addition, the specification also describes sixteen variants of SEQ ID NO: 1 with IRES activity in plants, including those set forth on page 6, paragraph [0025]. Of those variants, SEQ ID NOs: 7-13 are derived from tomato, antirrhinum, tobacco, rice, maize, *M. polymorpha*, and *Physcomitrella patens*, respectively (see paragraph bridging pages 6-7 of the specification). Applicants also submit that each of SEQ ID NOs: 7-13 comprise no more than 2 substitutions with respect to SEQ ID NO: 1. Thus, the specification provides written description support of the disclosed and claimed genus of polynucleotides.

Applicants further submit that the plants capable of use with the claimed polynucleotides, have also been described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the specification describes plants belonging to various

families including, but not limited to, tobacco, maize, rice, *etc.* (specification at, e.g., pages 15-16, paragraphs [0055]-[0056]). As set forth above, the specification also describes IRESes, some of which are derived from the very same plants. Moreover, the specification further describes that the claimed polynucleotides are capable of use in the plants described in the specification (see, e.g., pages 14-16, paragraphs [0050] – [0056]).

In response to the Office's assertions regarding the ECMV IRES, Applicants submit that the Office's assertion is not germane at least because (1) the claimed subject matter does not encompass the ECMV IRES; and (2) viral IRESes such as the ECMV IRES, and cellular IRESes, including those encompassed by the claimed subject matter, are distinct. In particular, as shown in Figure 4 on page 1540 of Chappell et al. (*P.N.A.S.* **97**:1536-1541, 2000; "Chappell"; see IDS submitted November 14, 2006), a cellular IRES maintains high activity in numerous cell types, whereas activity of an ECMV IRES was shown to be cell type-dependent. In addition, Chappell discloses that "...accumulated evidence indicates that viral and cellular IRESes may be fundamentally distinct" (page 1539, paragraph bridging first and second columns). Thus, contrary to the Office's assertion, at least with respect to cellular IRES function, there would not appear to be a high degree of unpredictability regarding IRES function as evidenced by Applicants' disclosure with respect to the effect on expression of the ECMV IRES.

In summary, Applicants submit that they have described the claimed subject matter, including the claimed polynucleotides and the plants in which such nucleotides may function, in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants further submit that contrary to the rejection as set forth in the Office Action dated

July 28, 2009, Applicants need not provide a working example for each and every embodiment encompassed by the claims in order to comply with the written description requirement.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the written description rejection under 35 U.S.C. §112, first paragraph.

The Office Action also rejects claims 1, 4, 5-9, 11, and 13 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Action alleges that that the specification, while being enabling for a polynucleotide comprising 10 repeats of SEQ ID NO: 1 that functions as an IRES in *Arabidopsis*, and a vector comprising said polynucleotide and a transformed *Arabidopsis* plant comprising said polynucleotide, does not reasonably provide enablement for a polynucleotide comprising DNA of SEQ ID NO: 1 or a DNA 'derived from' SEQ ID NO: 1, or for IRES activity in any plant other than *Arabidopsis*.

In particular, the Office Action asserts that Applicants' previous argument regarding the ability of one of ordinary skill in the art to make and use the invention without undue experimentation is not persuasive given the alleged evidence in the specification that an IRES functional in mammalian and tobacco systems, i.e., the ECMV IRES, did not function in *Arabidopsis* (Office Action at page 12, first full paragraph). Similarly, the Office did not find Applicants' arguments regarding the disclosure of detailed sequence structures persuasive, allegedly because the "the detailed structures referred to were not shown to have IRES function, this is merely a hypothetical assertions [sic]" (see Office Action, paragraph bridging pages 12-13). The Office Action also alleges that the "lack of working examples, taken together with the evidence that an IRES that functions in mammalian cells and tobacco cells did not function in

Arabidopsis...provides a fact pattern that does not support enablement through the broad scope of the instant claims." *Id.*

In response, Applicant submit that the specification provides sufficient guidance such that one of skill in the art could make and use the full scope of the claimed subject matter without undue experimentation. Initially, Applicants submit that the rejection is moot with respect to claim 5, which is cancelled.

Applicants further submit that the Office Action appears to improperly construe comparative examples provided in the specification as falling within the claimed subject matter or as representative of the claimed subject matter. In particular, Applicants submit that the specification at page 18, paragraph [0062] describes, for comparison, a vector comprising an ECMV IRES known to function in mammalian cells and tobacco. As attributed in the specification, this ECMV IRES was disclosed in Urwin et al. (*The Plant Journal* **24**(5):583-589, 2000; see IDS submitted November 14, 2006). As further described at page 21, paragraph [0073] of the specification, transgenic plants created with expression vectors comprising the ECMV IRES, denoted "ECMV-3," "ECMV-20," ECMV-26," and "ECMV-30," were compared to embodiments of the claimed subject matter and the results are disclosed, e.g., in Figure 4. In contrast, the specification describes transgenic plants, denoted "18S NS-2," "18S NS-15," "18S NS-23," and "18S NS-37," which were created by using an expression vector in which 10 repeats of the nucleotide sequence of SEQ ID NO: 1 without spacer sequences served as the IRES (page 21, paragraph [0072]). Indeed, the Office Action concedes as described in the specification, the effect on expression from the SEQ ID NO: 1 bearing construct was 'far increased' (Office Action at page 10, lines 12-17).

Thus, Applicants submit that it is improper to conclude, as the Office Action does, that comparative results associated with a virus-derived ECMV IRES are representative of the predictability with which the claimed subject matter will function. Indeed, the Office concedes that "[t]he ECMV IRES does not appear to be related to the instant invention of SEQ ID NO: 1..." (Office Action at page 10, lines 10-12). Furthermore, as set forth in the response to the written description rejection, above, viral IRESes such as the ECMV IRES, and cellular IRESes, including those encompassed by the claimed subject matter, are distinct. For example, as shown in Figure 4 on page 1540 of Chappell et al. (*P.N.A.S.* **97**:1536-1541, 2000; "Chappell"; see IDS submitted November 14, 2006), a cellular IRES maintains high activity in numerous cell types, whereas activity of an ECMV IRES was shown to be cell type-dependent. In addition, Chappell discloses that "...accumulated evidence indicates that viral and cellular IRESes may be fundamentally distinct" (page 1539, paragraph bridging first and second columns). Thus, contrary to the Office's assertion, at least with respect to cellular IRES function, there would not appear to be a high degree of unpredictability regarding IRES function as evidenced by Applicants' disclosure with respect to the effect on expression of the ECMV IRES.

Applicants further submit that the Office appears to be holding Applicants to an improper standard of enablement whereby Applicants' claims are alleged to be enabled only for the scope to which Applicants have disclosed working examples. Whether or not an Applicant's invention is enabled has been determined by the courts to involve several factors including the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See *In re Wands*, 858 F.2d 731, 737, 8

USPQ2d 1400, 1404 (Fed. Cir. 1988). In fact, there is no *per se* requirement for working examples, yet Applicants have provided a number, in addition to the remaining detailed description of the invention.

Applicants submit that the specification provides sufficient guidance such that one of skill in the art could make and use the full scope of the claimed subject matter without undue experimentation. Applicants submit that, e.g., the disclosure provides the detailed sequence structure for exemplary nucleic acids encompassed by the claims. The specification indicates particular nucleotides that can be modified and still retain IRES function (see SEQ ID NOs: 5-20, and paragraph [0024] on page 6). Applicants remind the Office that MPEP 2164.04 states that the examiner, not the applicant, has the "initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." Applicants further submit that "[a] specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." MPEP 2164.04. In other words, contrary to the Office's assertion, the embodiments described in the specification are not mere "hypothetical assertions," and should be taken as in compliance with the enablement requirement absent a reasonable basis to question the enablement provided for the claimed invention. Applicants submit that the Office Action fails to provide such reasonable basis.

Applicants further submit that the level of skill of one of ordinary skill in this field is high, and that in combination with the guidance provided by the specification and in view of the state of the art, e.g., as discussed above with respect to cellular vs. viral IRESes, one of ordinary skill in the art would have been able to practice the full scope of the claimed subject matter without undue experimentation.

Applicants also submit that the claimed invention is also enabled for at least the reasons set forth in Applicants' response to the rejection of the claims under 35 U.S.C. § 112, first paragraph (written description), e.g., the specification describes (1) along with SEQ ID NO: 1, sixteen variants with IRES activity in plants, including those set forth on page 6, paragraph [0025]; and (2) plants belonging to various families including, but not limited to *Brassicaceae* (e.g., thale-cress), *Poaceae* (e.g., maize), *Solanaceae* (e.g., tobacco), and *Leguminosae* (e.g., soybean) that are to be transformed and used with the disclosed IRES sequences.

Based on at least the foregoing, Applicants submit that the instant disclosure provides clear and sufficient guidance such that the claimed invention is enabled. Applicants respectfully request reconsideration and withdrawal of the rejections under the enablement requirement of 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims. Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

The Office is authorized to charge any required fee to Deposit Account No. 19-0089.

Should the Examiner have any questions regarding this response or this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
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December 24, 2009
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